

Application No. 10/076,071
Amendment dated April 20, 2006
Reply to Office Action dated October 20, 2005

Amendments to the Specification:

Please replace the paragraph appearing at page 41, lines 3-18, of the specification with the following amended paragraph:

Acidosis is present in, or plays a role in, a number of diseases and conditions, including hypoventilation, hypoxia, ischemia, prolonged lack of oxygen, severe dehydration, diarrhea, vomiting, starvation, AIDS, sepsis, kidney disease, liver disease, metabolic diseases (*e.g.*, advanced stages of diabetes mellitus), and neurodegenerative diseases (*e.g.*, Alzheimer's). Acidosis is also caused by certain medications (*e.g.*, large amounts of aspirin and oral medications used to treat diabetes), and instances of mild acidosis have been reported to increase with age (Knight, "Metal Heads," *New Scientist*, 8/26/00; <http://www.purdycenvironment.com/Full%20New%20scientist001.htm>). Under normal conditions, copper is bound to plasma proteins and peptides, primarily ceruloplasmin and albumin. In acidotic conditions, copper is released from the proteins to which it is normally bound. It is estimated that 40-70% of weakly bound copper is released at pH 6.0. Free copper can participate in reactions that lead to the formation of ROS and causes a number of other deleterious effects, such as interfering with metabolism and energy utilization. Thus, the metal-binding compounds of the invention may be used to treat diseases or conditions involving acidosis to prevent damage due to ROS, to prevent other deleterious effects of free copper, or both.